Current Clinical Studies and Patient Referral Procedure

The Warren Grant Magnuson Clinical Center

NIH Publication No. 86-217
Revised January 1986

U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

The Clinical Center
Bethesda, Maryland 20892

Key to Abbreviations Used in this Brochure

NCI	National Cancer Institute
NEI	National Eye Institute
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NIAAA	National Institute of Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases
NIADDK	National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases
NICHD	National Institute of Child Health and Human Development
NIDR	National Institute of Dental Research
NIMH	National Institute of Mental Health
NINCDS	National Institute of Neurological and Communicative Disorders and Stroke

The Clinical Directors

Institute		*Building/ Room**	*Telephone***
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The Clinical Center

John L. Decker, M.D. Director	10/2C124	(301) 496-4114

*NIH's mailing address is National Institutes of Health, Bethesda, MD 20892.

**Unless otherwise indicated, the area code for all telephone numbers in *Current Clinical Studies* is 301.

***Dr. Andres' address is Room 2B13, NIA Gerontology Research Center, Baltimore City Hospitals, 4940 Eastern Avenue, Baltimore, MD 21224.

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Contents

The Warren Grant Magnuson CLINICAL CENTER of the National Institutes of Health in Bethesda, Maryland, accepts a limited number of patients each month for study and therapy. Studies to which patients are currently being admitted are described briefly in this brochure. Patients are admitted only on referral by a physician or dentist.

The Clinical Center is a modern laboratory-hospital facility shared by the 11 institutes that conduct combined laboratory and clinical study programs. The patient care area is comparable in staff and equipment to that of the leading general hospitals, with special provisions for the comfort and welfare of patients with chronic diseases.

The cooperation and assistance of physicians and dentists in private practice and those associated with hospitals and clinics are essential in the proper selection of patients to participate in these studies. Patients should be referred and will be admitted on the basis of a diagnosis that meets the requirements for a particular study.

Referring physicians and dentists are welcome to visit their patients at the Clinical Center. When a patient is discharged, the referring physician or dentist receives a full report on the results of studies and the treatment given. Cooperation of physicians, dentists and patients is appreciated for the extended period of follow-up observation which is usually desirable after the patient has been returned to the care of the referring physician or dentist.

PROCEDURE FOR REFERRAL OF PATIENTS

To request admission of a patient, physicians and dentists should submit a letter of referral along with a brief summary of the medical history and current situation, including the diagnosis or diagnoses and the name, age, address and telephone number of the patient or parents, if the patient is a minor. Preliminary inquiries may be made by telephone. There are no "application forms" to be completed.

The size and complexity of NIH and the research mission of the institutes require that the clinical program be organized somewhat differently from that usually found in a university or other large general hospitals. For example, instead of one, there are several separate services for endocrinology, metabolic studies, childhood diseases, etc. Similarly, a given diagnosis may be of potential interest to investigators in two or even three institutes.

We have tried to provide a current listing in this brochure of studies under way at the Clinical Center and the individuals who handle referrals in each area. Physicians or dentists can address written referrals to:

Office of the Director
The Clinical Center
Building 10, Room 2C146
National Institutes of Health
Bethesda, MD 20892

Telephone inquiries from physicians and dentists regarding referrals are welcome. The physician may either call the institute contact listed in the brochure or the Patient Referral Service at (301) 496-4891.

It will often be desirable for prospective patients to be interviewed and examined by the Clinical Center physician or dentist to whom, or to whose institute, the patient has been referred.

If more than one physician or dentist is interested in receiving follow-up reports on the patient, their names and addresses should be indicated in the referral letter.

If necessary, the Social Work Department of the Clinical Center will assist prospective patients with

personal problems occasioned by their admission to the Center. The resources available to this department will not, however, permit financial assistance to individuals and their families except for certain types of emergency situations.

There is no charge to the patient for medical, surgical or other hospital services rendered as a necessary part of his or her participation in the research project. However, the patient's transportation costs usually cannot be paid by NIH.

ELIGIBILITY REQUIREMENTS

1. The patient's specific disease or other conditions must be under active investigation by National Institutes of Health physicians at the time of admission.
2. The patient must be referred by his or her own physician or dentist or by a qualified physician or dentist in a hospital, clinic or other medical organization.
3. Age, weight, sex, general health and length of an existing waiting list of qualified patients are factors that each institute takes into consideration. Possibilities for long-term inpatient status or extended followup observations, or both, may also be important criteria for admission. There are no residential or citizenship requirements. Apart from the medical considerations listed above, there are no other restrictions based on race, creed, age, sex or color.
4. The patient must have a reasonable understanding of his or her role in a research study and must be willing to participate.
5. Because of special procedures involved, the selection of noncompetent patients (for psychiatric studies) is limited at present almost entirely to individuals who are already patients at mental hospitals.

LENGTH OF STAY

All concerned should understand that admission to the Clinical Center is for research purposes only. Patients will be returned to the care of their referring physician or institution, or to their family, when their participation in a study has been com-

pleted and their medical condition permits. The clinical director of the institute in which a patient is under study is responsible for making these determinations.

CLINICAL STUDIES

The principal studies for which patients will be admitted during the current period, together with some of the more important diagnostic or other criteria, are described briefly in the following pages.

This listing is revised and reissued annually. On request, hospitals, clinics, medical schools, medical societies, medical journals and individual physicians and dentists will be placed on a mailing list to receive it as issued.

National Institute on Aging

REUBIN ANDRES, M.D.
Clinical Director

Telephone referrals of patients to Laboratory of Neurosciences studies may be directed to:

Angela M. Moore, MSW
Social Worker
(301) 496-4754

LABORATORY OF NEUROSCIENCES

Cerebral Metabolism in Dementia—At NIA's Section on Brain Aging and Dementia, a part of the Clinical Center of the National Institutes of Health in Bethesda, Maryland, scientists are involved in research activities focused primarily on **dementias** and associated neuropathologic diseases as these relate to the elderly. Studies look closely at **multi-infarct, Alzheimer's** type **senile dementia** and **Parkinson's** dementia. They also examine the **normal aging** process in 20- to 100-year-old individuals from a biochemical, cardiovascular and general physiological perspective which includes a careful evaluation of brain function. New technologies such as positron emission tomography (PET), are employed to look at brain metabolism in aging and dementia.

Patients with Down's syndrome and Fragile X syndrome are also needed for current studies.

National Institute on Alcohol Abuse and Alcoholism

MARKKU LINNOILA, M.D., PH.D.
Clinical Director

Telephone referrals of patients to the Laboratory of Clinical Studies may be directed to:

Yolande B. Davenport, MSW
Chief, Unit of Family Studies
(301) 496-9705

LABORATORY OF CLINICAL STUDIES

Chronic Organic Brain Syndromes of Alcoholism—Patients with brain dysfunction attributable to chronic alcohol comsumption will receive a complete neuropsychiatric evaluation including various specialized measures of brain function: neuropsychological tests, electroencephalographic studies, measures of neuroendocrine function, and brain imaging techniques, such as computerized axial tomography (CAT), positron emission tomography (PET), and nuclear magnetic resonance (NMR). Selected patients will be eligible to receive drug treatment designed to ameliorate cognitive and other behavioral signs and symptoms of chronic organic brain syndromes, such as neurotransmitter replacement, neuropeptides, or nootropic agents.

Family Studies—Families of alcoholic patients will be evaluated by a multidisciplinary team for various aspects of biopsychosocial functioning. Selected patients and their adult and child family members may be eligible for longitudinal studies with the aim to prospectively identify biological and social factors that may contribute to the development of alcoholism: cognitive development, neuropsychological functioning, electroen-

cephalographic techniques, and biochemical markers. Extensive family pedigrees will be constructed in order to evaluate genetic predisposing and protective factors in the development of alcoholism in individuals from high risk families. Selected patients may be eligible to participate in ongoing research psychotherapeutic treatment groups.

Pharmacologic Reduction of Alcohol Consumption—Patients who are medically healthy but have serious alcohol related problems and who wish to reduce their alcohol consumption may be eligible for long-term drug studies designed to reduce their craving for alcohol.

Treatment of Alcohol Withdrawal—Selected patients without serious medical problems who have been drinking prior to admission will be studied extensively in the hospital during their withdrawal from alcohol in order to better understand the alcohol withdrawal syndrome and to develop new and more efficacious pharmacologic treatments. During the studies, an attempt will be made to identify biological characteristics of patients which will serve as prognostic indicators of recovery of the brain and other organ system funciton: sleep electrophysiology, drug metabolism, neuropsychological function: sleep electrophysiology, drug metabolism, neuropsychological functioning, intermediary carbohydrate metabolism, neuroendocrine function and immune response.

National Institute of Allergy and Infectious Diseases

MICHAEL M. FRANK, M.D.
Clinical Director

Telephone referrals of patients to NIAID studies may be directed to:

Allergy and Infectious Diseases Consultant
(301) 496-4831

Acquired Immunodeficiency Syndrome (AIDS)—Patients with AIDS will be evaluated with regard to the natural history and clinical manifestations of the syndrome. Therapeutic protocols aimed at immunological reconstitution as well as treatment of the etiologic agent will be carried out.

Allergic rhinitis—Nasal responses to provocative challenge with mediators and allergens are being studied.

Anaphylaxis—Selected patients having recurring **anaphylaxis** or anaphylactoid reactions will be accepted into studies designed to enumerate the responsible mediators as well as improve therapy of this problem.

Asthma and Allergic Diseases—Selected patients with **bronchial asthma** and other **allergic diseases** are accepted for study. Of particular interest are **seasonal allergic asthmatics, aspirin-sensitive patients** and certain **"intrinsic" asthmatics.** Patients will undergo studies designed to characterize their immunologic, biochemical and neurophysiologic responses.

Autoimmune Hemolytic Anemias—Selected patients with **Coombs'-positive hemolytic anemia** will

be accepted for study of the immunologic aspects of their disease and the role of complement in its expression.

Chediak-Higashi Syndrome—The role of certain lysosomal enzymes in the pathogenesis of this disorder is under investigation. In addition, the function of the phagocytic system is measured.

Cold Urticaria—Patients who experience hives upon exposure to cold are being sought. Specific mediators released during cold challenge are being examined.

Cryptococcosis—Patients with untreated cryptococcosis are requested for study of diagnostic methods, immunologic responses and therapy with various promising drugs. Patients with suspected cryptococcosis (meningitis or disseminated disease) not proven by culture but with convincing negative workup for other causes will be considered.

Eosinophilic Syndromes (Loeffler's Syndrome, Loeffler's Endocarditis, Hypereosinophilic Syndrome, Polyarteritis with Eosinophilia, Tropical Eosinophilia, Eosinophilic Leukemia, Eosinophilic Collagen Vascular Disease, and Allergic Disorders with Eosinophilia—An intensive multidisciplinary study is under way to determine the pathophysiology of these diseases. Of special interest are patients with eosinophilic invasion of tissues, especially the heart, which is the most commonly involved organ. Cardiac involvement is the most frequent cause of morbidity and mortality. Several promising modes of therapy are being employed and studied in these patients.

Food Reactions—Selected patients with a clear history of an adverse reaction to a food or food additive will be studied to determine the reproducibility of the history, and the pathogenesis of the reaction.

Gluten-Sensitive Enteropathy (Coeliac Sprue)—Patients with gluten-sensitive enteropathy will be admitted for study of immunologic and genetic abnormalities present in this disease.

Granulomatous Diseases—A variety of immunological and biological functions in patients with **sarcoidosis, granulomatous hepatitis** and other **granulomatous diseases** are under study. In particular, the physiological capabilities of leukocytes are being investigated. Improved therapeutic regimens are being evaluated.

Especially needed are children with chronic granulomatous disease, which is characterized by recurrent pyogenic infections and granulomatous involvement of affected tissues, in order to further define the nature of the leukocyte defect responsible for the abnormal destruction of bacteria characteristic of this disease and to develop new therapeutic approaches.

Chronic Granulomatus Disease—Patients with **chronic granulomatous disease** will be admitted for studies of host defenses and assessment of the genetic basis of the disease. Long-term management of acute and chronic problems will be provided as needed.

Hereditary Angioneurotic Edema—Selected patients with **hereditary angioneurotic edema** will be admitted for studies of complement function and for trials of new therapeutic agents.

Herpes Simplex Virus Infections—Patients with recurrent, chronic, or severe **herpes simplex virus** infections are studied in outpatient or, if necessary, inpatient facilities. Viral pathogenesis and potential therapeutic measures are evaluated.

Hypocomplementemia—Selected patients with low or **absent serum complement** will be admitted for study of complement function.

Hypocomplementemic Glomerulonephritis—Studies of the role of complement and of factors which activate complement in the development of this disease will be conducted. Selected patients will be admitted for study.

Infectious Mononucleosis—Patients with histories compatible with recurrent or chronic **Epstein-Barr**

virus infections are being studied to assess the nature of their disorder and potential therapeutic measures.

Immunodeficiency Diseases—Selected patients with **immunodeficiency,** such as those with hyper-IgM syndrome, common variable immunodeficiency and selective IgA deficiency.

Inflammatory Bowel Disease— Patients with **inflammatory bowel disease (Crohn's disease or ulcerative colitis)** will be admitted for study of the role of immunologic factors in the causation of diseases and the effect on patient *in vitro* function of various therapeutic agents.

Mastocytosis and Urticaria Pigmentosa—Certain individuals with these diseases are being sought in order to assess the factors responsible for symptoms as well as the response to certain antihistamine and anti-mast-cell drugs.

Midline Granuloma and Wegener's Granulomatosis—Several immunologic and microbiologic studies are done on selected patients with these diseases. X-ray and immunosuppressive chemotherapy are being evaluated also.

Mucorrhea—Patients producing **excessive quantities of mucus** are being accepted for studies into both the pathogenesis and treatment of this problem.

Mycoses—Patients requiring therapy for aspergillosis, fungal sinusitis **histoplasmosis, blastomycosis** and **coccidioidomycosis** will be considered for treatment with oral ketoconazole, a new chemotherapeutic agents.

Parasitic Diseases: Amebiasis, Schistosomiasis, Filariasis, Trypanosomiasis (American and African), Malaria, Leishmaniasis, and Toxoplasmosis — In addition to the above, patients with other known or suspected **parasitic infections** will be considered for evaluation and study. In addition to research studies, specialized tests and procedures are available to diagnose and characterize parasitic

infections. All patients for whom treatment is available and indicated will be treated while hospitalized.

Paroxysmal Nocturnal Hemoglobinuria—Selected patients with this disorder will be admitted for studies of pathophysiology as well as better methods of diagnosis and therapy.

Recurrent Pyogenic Infections—Patients with **recurrent bacterial infections** will be admitted to study their host defense mechanisms, with particular emphasis on leukocyte functions. In particular, patients with **eczema, elevated IgE** and recurrent superficial and deep-seated **staphylococcal infections** are being evaluated for defective leukocyte function.

Sjogren's Syndrome—Selected patients with **Sjogren's** syndrome will be admitted either as inpatients or outpatients for the purpose of conducting studies related to the immunologic abnormalities associated with this disease. Specifically, the mechanisms of B-lymphocyte hyperreactivity and immunoregulation will be studied. In addition, potential therapeutic measures will be evaluated where applicable.

Urticarial and Leukocytoclastic Vasculitis—Selected patients will be admitted for study.

Varicella-Zoster Infections— Selected individuals with **varicella-zoster infections** are evaluated in outpatient or, if necessary, inpatient facilities. Viral pathogenesis and potential therapeutic measures are studied.

Vasculitis—Selected patients with disseminated **vasculitis, hypersensitivity angiitis** and other forms of **inflammatory vascular diseases** will be accepted for study of various *in vivo* and *in vitro* immunologic parameters before, during and after treatment with corticosteroids and/or cytotoxic agents.

Vasomotor rhinitis—(See allergic rhinitis).

Weber-Christian Disease—Patients with **relapsin**
nodular panniculitis (Weber-Christian disease) ar
under study in order to delineate the pathophysio
logic mechanisms in this puzzling inflammator
disease as well as to design appropriate therapeuti
regimens.

National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases

PHILLIP GORDEN, M.D.
Clinical Director

Telephone referral of patients to NIADDK studies may be directed to the individuals listed under each subject area.

Abnormalities in ADH (Antidiuretic Hormone, Vasopressin) Secretion—Complete diagnosis and therapy are offered to patients with normal BUN or NPN who have (1) **diabetes insipidus**, or (2) inappropriate or excessive ADH secretion or (3) defective control of thirst or water intake or urine volume and specific gravity or serum sodium concentration. A new sensitive immunoassay has been developed to assist in diagnosis. Many of these patients also have **intracranial or intrathoracic tumors.**—Phillip Gorden, M.D., (301) 496-4181.

Blood Diseases—Immunological aspects of **thrombocytopenia, anemia,** and **granulocytopenia** are under investigation. Sera of patients with suspected **drug** sensitivity are sought for testing. Individuals who develop severe thrombocytopenia about 1 week after blood transfusion **(post-transfusion purpura)** are of particular interest. New approaches to therapy of acute and chronic **idiopathic thrombocytopenic purpura** (ITP) and of congenital and acquired **platelet abnormalities,** particularly **thrombasthenia,** are evaluated. Sera and platelets of mothers who have had **thrombocytopenic** or **leukopenic infants** are sought for appropriate antibody tests to evaluate maternal-fetal incompatibility antenatally or postnatally. Studies are being done on the biochemistry of blood coagulation and on platelet function, with particular reference to the development of better

forms of therapy for various congenital and acquired **hemorrhagic** and **thrombotic diseases. Patients with thrombasenia and Bernard-Soulier syndrome,** as well as obscure undiagnosed **bleeding disorders,** will be considered for admission to the Clinical Center.—N. Raphael Shulman, M.D., Clinical Hematology Branch, (301) 496-4787.

Chronic Type B Hepatitis (HBsAg-Postive)—Persons with **chronic type B hepatitis** are being accepted into studies of anti-viral therapy of this disease. Patients should be between the ages of 18-65 and should be without other significant medical illnesses. Patients will initially be evaluated in the outpatient clinics of the National Institutes of Health, in order to assess the chronic hepatitis disease activity and the status of hepatitis B virus in the serum. Patients with high titers of virus and active disease will be offered the chance to enter into a randomized controlled trial of an antiviral therapy.—Jay H. Hoofnagle, M.D. and E. Anthony Jones, M.D., Liver Diseases Section, (301) 496-1721.

Diabetes Mellitus—Patients are 6-60 years who fall into the following categories will be considered for study.

1. Patients of approximately normal weight with abnormal glucose tolerance who have never received insulin or have been insulin treated for less than 4 weeks.
2. Thin or obese **diabetics** who have never received insulin or who have been insulin treated for less than 4 weeks.
3. Both insulin-treated and non-insulin-treated patients with **insulin resistance** (patients with high endogenous insulin concentrations or patients who usually require more than 200 units per day of exogenous insulin). This would include patients with **lipoatrophic diabetes,** syndrome of **insulin resistance associated with acanthosis nigricans, acromegaly, Cushing's disease** and excess antibody production.

4. Patients with **diabetes** and evidence of other **endocrine disorders** such as **hypothyroidism, adrenal insufficiency,** or **hirsutism.**

5. Patients with **hyperglycemia** and symptoms of an autoimmune disorder.

Severely ill patients may be referred by a direct telephone call to Phillip Gorden, M.D., (301) 496-4181, or Simeon Taylor, M.D., Diabetes Branch, (301) 496-4658.

Gastrointestinal Diseases—The Gastroenterology Section is interested in conferring with outside physicians involved in the care of any problem in gastroenterology that is unusual because of its rarity, complexity, associated features or family distribution. Of particular interest are patients with (1) **Zollinger-Ellison syndrome,** or (2) **secretory diarrhea.** Zollinger-Ellison patients who have disseminated tumor or who are unsuitable for surgery are of special interest, as are all patients with atypical or refractory **peptic ulcers.**—Jerry D. Gardner, M.D., and Robert T. Jensen, M.D., Gastroenterology Section, (301) 496-4201.

Gynecomastia with Carcinoma—Some men with **cancer** develop enlarged breasts, and we are interested in studying the etiology of their **gynecomastia.** In fact, gynecomastia may precede clinical recognition of the neoplasm. Patients with unexplained gynecomastia who are chronic smokers or who have cancer will be considered for study and treatment (surgery, radiotherapy, chemotherapy). —Bruce Weintraub, M.D., (301) 496-3405, Clinical Endocrinology Branch.

Hyperthyroidism with Carcinoma—Some patients with **cancer** develop increased concentrations of protein-bound- and thyroxine-iodine in their serum, typically unaccompanied by the usual physical findings of **hyperthyroidism.** In certain instances this may be due to production by the neoplasm of an ectopic thyroid-stimulating hormone. Patients with this association are of interest for this study.—Bruce Weintraub, M.D., Clinical Endocrinology Branch, (301) 496-3405.

Hypoglycemia—Selected patients age 16 and over who have had fasting blood glucose of 45mg/100ml or less will be studied and treated. We are particularly interested in hypoglycemic patients who have large **intrathoracic and intra-abdominal tumors** which do not secrete excess insulin. Additionally, we are interested in patients with insulin-secreting **tumors of the pancreas.** We are also interested in states of fasting hypoglycemia of unknown etiology. Reactive (post-prandial) **hypoglycemia,** unless extraordinarily severe and well documented, is not being studied.—Phillip Gorden, M.D., (301) 496-4181, and Simeon Taylor, M.D., Diabetes Branch, (301) 496-4658.

Hypogonadism—Men or women over 16 years of age with primary or secondary **gonadal failure,** untreated during the previous six months, will be given extensive clinical, laboratory, and radiologic evaluation for associated endocrinopathies. Secretion of the pituitary polypeptide hormones and their subunits will be studied using the recently described synthetic releasing agents (TSH-RH, LH-RH).—Bruce Weintraub, M.D., (301) 496-3405, Clinical Endocrinology Branch.

Non-puerperal Lactation—Selected patients with inappropriate **(non-puerperal) lactation** will be admitted for study. Patients—male or female—with **galactorrhea** will receive full endocrinologic evaluation.—Bruce Weintraub, M.D., (301) 496-3405, Clinical Endocrinology Branch.

Parathyroid Disorders and Metabolic Bone Diseases—Radioimmunoassays for parathyroid hormone in plasma and determination of cyclic AMP excretion in the urine have increased diagnostic accuracy for **hypo-** and **hyperparathyroid** states. Patients with **hypercalcemia, hypophosphatemia, nephrocalcinosis, nephrolithiasis, multiple endocrine adenomatosis** or other manifestations of hyperparathyroidism are sought. Patients with hypercalcemia of unknown cause are also sought. Recent use of noninvasive imaging techniques and of selective venous catheterization combined with radioimmunoassay for parathyroid hormone has allowed localization of **adenomas** before surgery.

This procedure has proved of particular value in localizing tumors incompletely removed at earlier surgical explorations and should be of use in diagnosing parathyroid hormone production by non-parathyroid tumors. Occasional parathyroid adenomas are suitable for deliberate ablation by transcatheter perfusion with vaso-occlusive agents. A selected series of patients with mild asymptomatic hyperparathyroidism is being studied prospectively in the clinic. Related methods are applied in selected cases of hypoparathyroidism, **rickets, osteomalacia,** vitamin D-resistant rickets, **juvenile osteoporosis, Zollinger-Ellison** syndrome and certain other abnormalities of bone metabolism. Patients with hereditary hypocalcemic rickets with or without alopecia are being sought. Patients with familial hypocalciuric hypercalcemia do not benefit from subtotal parathyroidectomy but are sought for evaluation and investigation.

Recent research has proven that parathyroid function importantly influences urinary excretion of cyclic 3′, 5′-AMP and that this nucleotide is involved in the mechanism of action of the hormone. Renal excretion of cyclic 3′, 5′-AMP has been developed into a useful diagnostic index for hyper- or hypoparathyroidism. Other investigations suggest that a constitutional defect of the hormonally sensitive enzyme adenylate cyclase may be the cause of **pseudohypoparathyroidism;** more patients with this disorder are needed for study.

Subtotal parathyroidectomy for parathyroid hyperplasia or definitive removal of parathyroid lesions after previous parathyroid surgery carries a high risk of postoperative hypoparathyroidism. We are investigating the use of autotransplantation of the patient's parathyroid tissue using either fresh or cryopreserved tissue depending upon clinical indicators.

Acquired osteomalacia without renal disease is occasionally associated with **benign or malignant mesenchymal tumors.** Patients with acquired osteomalacia are sought. Selected patients with juvenile osteoporosis are also sought.—G.D. Aurbach, M.D., S.J. Marx, M.D., and A.M. Spiegel, M.D., Metabolic Diseases Branch, (301) 496-5051.

Management of Rheumatoid Arthritis of the Foot—Foot discomfort represents a substantial disability, and the eventual outcome is immobility. Currently, podiatric intervention has been attempted with some success in relieving pain and delaying surgery. Patients with definite or classical adult onset **rheumatoid arthritis** who have foot pain, without severe deformities, will be acceptable for study. In an attempt to assess the impact of these procedures on the natural history of the foot deformity, the department will offer special shoeing techniques.—Lynn H. Gerber, M.D., (301) 496-4733, and John H. Klippel, M.D., (301) 496-3374, Arthritis and Rheumatism Branch.

Pituitary Tumors and Hypopituitarism—**Pituitary tumors** with growth hormone hypersecretion (**acromegaly** or **gigantism**) are being studied and evaluated for therapy with transsphenoidal surgery, supervoltage irradiation and bromergocryptine. In addition, patients with **chromophobe adenomas** (with or without galactorrhea) and various forms of **anterior pituitary insufficiency** are under study, including cases of isolated growth hormone deficiency or patients with apparently normal growth hormone but growth retardation or growth excess. **Tumors of the hypothalamus and pineal** may be associated with hypopituitarism and/or diabetes insipidus. Patients suspected of having such tumors are sought for diagnosis, study, and therapy.—Phillip Gorden, M.D., (301) 496-4181, and Simeon Taylor, M.D., Diabetes Branch, (301) 496-4658.

Polymyositis and Dermatomyositis—The immunologic and possible virological pathogenesis or **polymyositis** and **dermatomyositis** is under active study. Patients at the very onset of their illness are particularly being sought. Selected patients at other stages of the illness will also be considered for clinical therapeutic trials.—Paul H. Plotz, M.D., Arthritis and Rheumatism Branch, (301) 496-3375.

Primary Biliary Cirrhosis—Selected patients with **primary biliary cirrhosis** are admitted for diagnostic evaluation, studies of copper metabolism, com-

plement and immune function and review of therapy. Patients are offered the opportunity to participate in a randomized controlled trial of an immunosuppressive therapy for this disease.—E. Anthony Jones, M.D., Liver Diseases Section, (301) 496-1721.

Psoriatic Arthritis—Selected patients with **psoriasis** and **arthritis** are admitted for research study. Clinical examination, blood tests and x-ray evaluation will be done. Investigations on blood and synovial tissue specimens will attempt to better characterize the immune pathogenesis of this disease. Patients with arthritis unresponsive to conventional therapies will be considered for participation in trials of investigational forms of treatment.—Lynn A. Gerber, M.D., (301) 496-4733, Ronald L. Wilder, M.D., and John H. Klippel, M.D., Arthritis and Rheumatism Branch, (301) 496-3374.

Kidney Diseases—Selected patients with immunologically-mediated glomerulonephritis are admitted for study of humoral and cellular immune functions. Patients with **Goodpasture's syndrome** and idiopathic **rapidly progressive crescentic glomerulonephritis** are sought for controlled clinical trials of certain immunosuppressive drugs and plasmapheresis.—James E. Balow, M.D., Howard A. Austin, III, M.D., and David Webb, M.D., Kidney Disease Section (301) 496-3092.

Rheumatoid Arthritis—The gradual destruction of cartilage, bone, and periarticular supporting tissues, which is characteristic of **rheumatoid arthritis,** results from the invasion of these structures by inflammatory granulation tissue. Research studies are attempting to better characterize immune abnormalities in the peripheral blood and synovial tissues of patients with this disease.

Selected patients with sustained polyarthritis who are unresponsive to conventional treatments will be considered for participation in clinical trials of investigational forms of therapy.—Ronald L. Wilder, M.D., Paul H. Plotz, M.D., Alfred D. Steinberg, M.D., and John H. Klippel, M.D. Arthritis and Rheumatism Branch, (301) 496-3374.

Systemic Lupus Erythematosus—Selected patients with systemic lupus erythematosus are admitted for research studies evaluating the autoimmune basis of this disease. Investigations of cellular immune activation and function are performed on peripheral blood, bone marrow, and lymph node cells. The relationship between immune complex handling and reticuloendothelial function is being assessed. Classical genetic studies are complemented by molecular biological analyses.

The efficacy and toxicities of several immunosuppressive drug regimens in the management of patients with lupus nephritis is being evaluated by controlled, randomized trials.—Alfred D. Steinberg, M.D., James E. Balow, M.D., Paul H. Plotz, M.D., Howard A. Austin, M.D., and John H. Klippel, M.D., Arthritis and Rheumatism Branch, (301) 496-3374.

Thyroid Diseases—Patients with various types of **goiter, thyroid nodules, thyroid carcinoma, thyroiditis, hypothyroidism** (especially if associated with goiter), **hyperthyroidism, exophthalmos** and **pretibial myxedema** may be accepted for study. Current studies especially require patients with functional metastatic **thyroid carcinoma** and patients with severe exophthalmos of **Graves' disease**. When clinically indicated, definitive medical or surgical treatment may be carried out at the Clinical Center.—Jacob Robbins, M.D., (301) 496-5761, and Bruce Weintraub, M.D., (301) 496-3405, Clinical Endocrinology Branch.

Inappropriate Secretion of TSH, Hypothyroidism—We are interested in evaluating patients whose serum concentration of thyrotropin (TSH) does not appear to be appropriate for their clinical status and circulating levels of thyroid hormones. Such patients include those with **hyperthyroidism** and detectable TSH, or those with resistance to the action of thyroid hormone.

We are also interested in patients with any form of **hypothyroidism,** particularly those with TSH deficiency and those who apparently require high doses of thyroid hormone replacement.—Bruce D. Weintraub, M.D., Clinical Endocrinology Branch, (301) 496-3405.

Tumors With Endocrine Function—Selected patients with **tumors** of any site who appear to have **excessive secretion of growth hormone, ACTH, TSH, vasopressin or insulin** will be studied. Selected patients with functioning **pancreatic islet cell tumors** associated with gastric hypersecretion **(Zollinger-Ellison syndrome)** or with the **pancreatic cholera** syndrome will also be considered for study.—Phillip Gorden, M.D., and Simeon Taylor, M.D., Diabetes Branch, (301) 496-4658.

Zollinger-Ellison Syndrome—Patients with recurrent, ectopic, multiple, or typical **peptic ulcers** associated with **gastric hypersecretion, or diarrhea or hypergastrinemia** will be admitted for diagnostic studies and therapy. Those already known to have **Zollinger-Ellison syndrome** will also be considered. Irrespective of their stage of disease or previous treatment, and depending on the precise assessment, patients will be assigned to one of two therapies: (1) H_2-histamine receptor blocking agents for control of their secretory problem, or (2) chemotherapy for those with extensive tumor or metastatic disease.—Jerry D. Gardner, M.D., and Robert T. Jensen, M.D., Gastroenterology Section, (301) 496-4201.

Hemoglobinopathies—Several noninvasive methods to characterize **blood flow abnormalities** in patients with sickle cell anemia and related syndromes (S-β-thalassemia, hemoglobin SC or SD disease) are presently under active investigation. Patients accepted for evaluation will undergo detailed hematologic and ophthalmologic assessment. Selected patients may undergo further studies, including whole body NMR imaging, laser-Doppler velocimetry and/or PET scanning, before and after various conventional and investigational modes of therapy. These studies are being conducted to develop more objective means to assess the severity of sickle cell anemia and to follow the results of therapy.—Alan N. Schechter, M.D. Griffin P. Rodgers, M.D., Laboratory of Chemical Biology (301) 496-5408.

National Cancer Institute

VINCENT T. DEVITA, JR., M.D.
Clinical Director
SAMUEL BRODER, M.D.
Deputy Clinical Director

Telephone referrals may be directed to the individuals listed under each branch.

BIOLOGICAL THERAPEUTICS BRANCH

Ronald G. Steis, M.D.
Chief, Clinical Investigations Section
(301) 695-1520

The Biological Therapeutics Branch of the Biological Response Modifiers Program is devoted to the clinical testing of biological agents and their integration with combination chemotherapy in the treatment of **cancer**. The agents being examined in detail include immunoaugmenting and immunomodulatory agents, lymphokines, interferon, maturation and differentiation factors, antitumor monoclonal antibodies and antitumor effector cells. The clinical research facilities of the Biological Therapeutics Branch are located both in the Clinical Center and in Frederick, MD, in conjunction with the National Cancer Institute's Frederick Cancer Research Facility. There is an inpatient unit located in Frederick Memorial Hospital as well as an outpatient facility, including a cytapheresis unit, located near the hospital. Both units are staffed by NCI oncologists and research nurses.

Current studies are focused on early clinical testing of interferon and antitumor monoclonal antibodies, lymphokines, and lymphokine activated killer cells and monocytes. The trials are open to patients with histologically proven **recurrent cancer** of any type and who have been refractory to curative therapy. In addition, patients must be ambulatory and not have received

chemotherapy, radiation, or corticosteriod therapy within four weeks of entering the trial. Currently, the trials are open to patients with **chronic lymphocytic leukemia, cutaneous T-cell lymphoma,** colon cancer, ovarian cancer, malignant lymphoma, hairy cell leukemia, and disseminated melanoma.

Patients entering research trials of the Biological Therapeutics Branch will be referred back to their primary physician after the completion of the trial for ongoing care and follow-up. While patients are under the care of the Biological Therapeutics Branch, research funds will be made available to help defray hospitalization and travel expenses for the necessary completion of a protocol.

DERMATOLOGY BRANCH

Chief: Stephen I. Katz, M.D., Ph.D.
(301) 496-2481

Selected patients with the following diseases will be admitted for study:

Benign Mucosal Pemphigoid (ocular pemphigoid)

Bullous Pemphigoid

Dermatitis Herpetiformis

Epidermodysplasia Verruciformis (genetic predisposition for flat warts and squamous cell carcinoma)

Epidermolysis Bullosa Acquisita

Erythema Elevatum Diutinum

Erythema Multiforme

Herpes Gestationis

Lamellar Ichthyosis

Multiple Warts

Pemphigus Foliaceus

Pemphigus Vulgaris

Pruritic Urticarial Papules and Plaques of Pregnancy

Psoriasis

Sezary Syndrome

Skin Cancer—Selected patients with extensive cutaneous **basal cell carcinoma** will be admitted for study and investigative therapy.

Tuberous Sclerosis

Vasculitis

Xeroderma Pigmentosum—Selected patients will be admitted for treatment, study and long-term follow up.

EPIDEMIOLOGY PROGRAM

Chief: Joseph F. Fraumeni, Jr., M.D.
(301) 496-1611

Persons with **cancer** or at high risk of any type of cancer are sought for studies of the causes of cancer. On referral, patients are considered for inclusion in studies because of:

1. a strong family history of malignant or benign neoplasia of an unusual type, pattern or frequency (e.g., three or more close relatives with cancer, particularly melanomas, sarcomas, lymphoproliferative neoplasms, ovarian and renal carcinomas); or
2. known or suspected factor(s) that predispose to neoplasia: either environmental exposures (occupation, drugs, radiation, diet, viruses, etc.) or genetic and/or congenital factors (Mendelian traits associated with neoplasia, birth defects and chromosomal anomalies); or
3. a tumor presenting with peculiar demographic or clinical features, such as unusual age of onset, bilaterality, unusual histopathology or response to therapy, or associated medical conditions, like autoimmune disease or immune deficiency; or
4. documented history of T-cell **leukemia** and/or **lymphoma** for study of human T-cell leukemia/lymphoma virus HTLV type I; or

5. an elevated risk of the acquired immune deficiency syndrome (AIDS) to evaluate the predisposition to certain cancers (e.g. Kaposi's sarcoma) and the role of viral infections, particularly with HTLV type III.

Studies consist of 1) verifying the patient's personal and family history by means of questionnaire, interview and review of records and histologic slides and, sometimes, 2) offering the opportunity for an in-depth clinical and laboratory evaluation to clarify the mechanism of carcinogenesis. Study may involve drawing blood, skin biopsy and radiographic examinations, as well as use of clinically available tissue for laboratory assays. No therapy beyond counseling is offered, but referral to other clinical branches of the National Cancer Institute will be expedited.

IMMUNOLOGY BRANCH

Chief: David H. Sachs, M.D.
(301) 496-5461

Immunotherapy and Immunobiology of Neoplastic Disease—The role of adjuvant immunotherapy is being evaluated in patients between the ages of 15 and 70 with **malignant melanoma.** Patients with Stage I (level IV or V) or Stage II disease who have been or can be surgically rendered free of clinical disease are candidates for this protocol. Initial evaluation includes clinical and laboratory staging as well as assessment of each patient's immune status. Patients are randomly assigned to treatment with adjuvant immunotherapy, chemotherapy or no further treatment. During follow up, they are monitored for evidence of antibody and cell-mediated immune responses to melanoma cells, in parallel with clinical and laboratory monitoring for evidence of tumor recurrence. In addition, the nature of the immunologic response of patients to selected tumors other than melanoma is under investigation. No futher patient accrual is anticipated.

Treatment of Malignant Disease by Allogenic Bone Marrow Transplantation—The feasibility of utilizing bone marrow from an unrelated, MHC-

unmatched donor for hematopoietic rescue following high dose chemotherapy and radiotherapy as treatment for aggressive malignancy is under evaluation. The protocol is open to untreated patients with malignant disease for which no conventional therapy is efficacious or treated patients with malignant disease for which such therapy has failed. Initially, only patients in the pediatric age group will be recruited; all patients must fail to meet criteria for entry into routine allogeneic or autologous bone marrow transplantation protocols. After an evaluation which includes staging and determination of baseline immunologic function, the patient will be treated with total body irradiation and combination chemotherapy followed by the administration of allogeneic MHC-unmatched marrow. Such marrow will be treated to eliminate T cell contamination; only marrows with satisfactory T cell depletion will be used. After marrow infusion, follow-up studies will include those tests which are routinely clinically necessary in this setting, including those related to graft versus host disease, those useful in understanding the competence of the reconstituting immune system, and restaging.

MEDICINE BRANCH

Chief: Robert C. Young, M.D.
(301) 496-4916

Patients with the following diseases are eligible for admission to the Medicine Branch for experimental treatment, provided they have not received prior chemotherapy or, where indicated, prior radiotherapy. A serious underlying illness in addition to the patient's neoplasm will disqualify the patient from eligibility for these studies.

Hodgkin's Disease and Non-Hodgkin's Lymphoma—Patients with biopsy-proven diagnosis of **Hodgkin's disease** or **non-Hodgkin's lymphoma** not previously treated are eligible for admission and treatment in collaboration with the Radiation Oncology Branch.

Ovarian Carcinoma—Patients who have epithelial **tumors of the ovary** are eligible for this program.

All stages of disease are acceptable, provided patients have had no prior chemotherapy or radiotherapy.

Breast Carcinoma—Patients with disseminated **breast cancer**, and with evaluable metastatic lesions, are eligible for admission for chemotherapeutic trials. Patients are excluded if they have received prior chemotherapy with more than one agent. Patients will also be accepted for evaluation and treatment of primary breast masses. Primary treatment protocols consist of a comparison of breast irradiation and lymph node dissection vs. modified radical mastectomy.

Testicular Carcinoma—Patients with poor prognosis bulky non-seminomatous **testicular cancer** metastatic to abdominal lymph nodes or distant sites are eligible for this study if they have received no prior radiotherapy or chemotherapy. In addition, patients with bulky disseminated **seminoma** may be admitted for combined modality therapy.

Cervical Carcinoma—Patients who have had no prior radiation or chemotherapy are eligible provided they have invasive **carcinoma of the cervix** *and* para-aortic lymph node involvement.

AIDS/Kaposi's sarcoma—Patients who develop Kaposi's sarcoma in the context of AIDS may be admitted for experimental therapy.

Pheochromocytoma—Patients who have biopsy-proven **pheochromocytoma** with metastatic and/or unresectable disease are eligible provided they have not had chemotherapy or are not receiving irradition.

METABOLISM BRANCH

Chief: Thomas A. Waldmann, M.D.
(301) 496-6653

Agammaglobulinemia—Selected patients with X-linked **agammaglobulinemia** and **thymoma** and agammaglobulinemia are being studied.

Antibody Deficiency with Normal Immunoglobulins—Selected patients with **recurrent infections,** normal immunoglobulin levels, but the inability to produce specific antibodies are being studied.

Ataxia-Telangiectasia—Patients with **ataxia-telangiectasia** are admitted for thorough evaluation as well as intensive study of immunologic function.

DiGeorge Syndrome (Thymic-Parathyroid Aplasia)—Selected patients with the **DiGeorge syndrome** are being admitted for study and therapy.

Growth Hormone Deficiency—Selected patients 4 to 20 years of age with isolated **growth hormone deficiency** or growth hormone deficiency as part of **panhypopituitarism** are being studied.

Hyper IgE Syndrome— Selected patients with recurrent severe bouts of **furunculosis** and **pneumonia** secondary to *Staphylococcus aureus* from early infancy and markedly elevated serum IgE levels are being studied.

Hypogammaglobulinemia—Patients with common, variable **hypogammaglobulinemia** and with different forms of **dysgammaglobulinemia** are being studied.

Isolated IgA Deficiency—Selected patients with isolated **IgA deficiency** or IgA deficiency associated with autoimmune disorders are being studied.

Serum Protein Abnormalities—Protein metabolism is being studied in patients with congenital and acquired **disorders of the serum proteins,** including subjects with idiopathic **hypoproteinemia,** gastrointestinal protein loss, **intestinal lymphangiectasia, allergic gastroenteropathy** and **analbuminemia.**

Severe Combined Immunodeficiency—Selected patients with the **severe combined immunodeficiency syndrome** are being admitted for study and therapy.

Cutaneous T-Cell Lymphomas (Sezary Syndrome) and adult T-cell leukemia—Selected patients with **cutaneous T-cell lymphomas** and high circulating neoplastic cell counts are being admitted for study, and when indicated, chemotherapy will be given in collaboration with the Division of Cancer Treatment.

Wiskott-Aldrich Syndrome—Patients are admitted for extensive evaluation of their immunodeficiency state. Selected patients are being evaluated in terms of their response to transfer factor therapy.

NCI-NAVY MEDICAL ONCOLOGY BRANCH

Chief: John D. Minna, M.D.
(301) 295-0097, (301) 496-0901, (301) 295-5402

Military and non-military patients with certain neoplastic diseases may be referred to this branch for primary treatment protocols. Various clinical and basic research programs are conducted. Combination chemotherapy, radiation therapy and immunotherapy are under clinical investigation. In addition, basic research in tumor cell biology, genetics, cytogenetics and immunology is conducted on clinically available material.

Non-military and military patients with **non-small cell and small cell lung cancer** and **mycosis fungoides/Sezary syndrome** are of particular interest.

Patients accepted for study and treatment in these programs will be admitted to the NCI-NAVY Medical Oncology Branch research ward at the Naval Hospital across the street from the main NIH campus.

PEDIATRIC BRANCH

Chief: Philip A. Pizzo, M.D.
(301) 496-4256

The Pediatric Branch accepts patients with selected neoplasms who are between 1 and 25 years of age. In most situations, patients must be previously untreated to be eligible for active protocols. All patients accepted for admission to this branch may be

enrolled in studies of optimal supportive care techniques. Selected patients are considered for autologous marrow rescue after high-dose chemotherapy. Clinically available materials are employed in basic studies of molecular biology, kinetics, cell biology, biochemistry, immunology and genetics.

Acute Leukemia—Untreated patients, usually under 25 years of age, will be considered for admission. In patients with **acute lymphocytic leukemia**, the therapeutic emphasis is on the evaluation of drug combinations, new agents and various methods for cranial prophylaxis.

Ewing's Sarcoma—Previously untreated patients with a biopsy-proven diagnosis are eligible for admission and treatment with radiation and chemotherapy. Patients at high risk for relapse are offered high-dose chemotherapy, total-body irradiation, and maximum supportive care.

Non-Hodgkin's Malignant Lymphoma (especially Burkitt's Lymphoma)— Patients under 25 years of age with a suspected or proven diagnosis of **non-Hodgkin's lymphoma** are being sought. While untreated patients are preferred, selected treated patients may be accepted. The treatment emphasis is on combined modality therapy including surgery, radiation and chemotherapy.

Osteogenic Sarcoma—Previously untreated patients with non-metastatic disease are offered surgery and adjuvant chemotherapy in conjunction with the Surgery Branch. Patients with metastatic disease, with or without previous treatment, are considered for admission at any age.

Rhabdomyosarcoma and Undifferentiated Sarcomas—Previously untreated patients with extensive disease, are considered for admission. Combined modality therapy will be evaluated.

RADIATION ONCOLOGY BRANCH

Chief: Eli Glatstein, M.D.
(301) 496-5457

Breast Cancer—Patients with Stage I or II **breast cancer** will receive either radical mastectomy or primary radiotherapy to the breast. This study is performed in collaboration with the Surgery and Medicine Branch. Early breast cancer studies involve randomization between radiotherapy and operative therapy.

Unresectable Sarcomas of Any Histologic Type—Patients with locally unresectable tumors will receive radiation therapy and radiosensitizers.

Gliomas—Patients without prior radiation therapy are eligible for a variety of radiotherapy studies performed in conjunction with the Neurological Surgery Branch of NINCDS.

Hodgkin's Disease—Patients with previously untreated disease are eligible for full staging and therapy with radiation and/or combination chemotherapy. This study is performed in collaboration with the Medicine Branch.

Malignant Lymphoma of Non-Hodgkin's Type—Patients with a biopsy-proven diagnosis of **lymphoma** are eligible for admission and treatment if they have had no prior treatment.

Oat Cell Cancer—Patients with biopsy-proven **oat cell carcinoma of the lung** are eligible for admission and treatment. This study is performed in collaboration with the NCI-NAVY Medical Oncology Branch.

Gastric Cancer—Patients with these neoplasms who have no distant metastases are eligible for studies involving intraoperative irradiation in conjunction with radical surgery performed by the Surgery Branch.

Carcinoma of the Nasopharynx—Patients without distant hematogenous metastases are eligible for studies of radiotherapy in conjunction with experimental radioprotecting agents.

Carcinoma of the Bladder—Patients without distant hematogenous metastases are eligible for

studies dealing with phototherapy and/or interstitial irradiation in conjunction with urologists in the Surgery Branch, NCI.

SURGERY BRANCH

Admitting Officer: David N. Danforth, Jr., M.D. (301) 496-1534

Sarcomas of Bone and Soft Tissues—Patients with high grade sarcomas of either the extremity, trunk, or head and neck, who have had biopsies and may or may not have had definitive surgical therapy are eligible for admission for treatment with new radiotherapeutic and chemotherapeutic adjuvant combined modality protocols. Patients with low grade sarcomas of either the extremity, or the trunk who have had biopsies and may or may not have had definitive surgical therapy are eligible for admission for treatment under combined surgery and radiation therapy protocols. Studies are also in progress evaluating new immunotherapeutic regimens for the treatment of selected patients with sarcoma who have not responded to standard treatments.

Patients with high grade osteogenic sarcomas of the extremity are eligible for treatment under combined surgery and chemotherapy protocols.

Colorectal Neoplasms—Patients with solitary or multiple hepatic metastases will be considered for hepatic resection, adjuvant intraperitoneal chemotherapy or chemotherapy by hepatic artery infusion. Immunotherapeutic trials involving intraperitoneal administration of hematopoietic cells are in progress for selected patients with peritoneal metastases from **colon and rectal cancer.** Patients with primary or recurrent rectal cancer will be considered for trials evaluating combined modality therapy.

Breast Cancer—Patients with untreated, stage I-II epithelial **cancers of the breast** as well as patients with suspicious breast masses which require biopsy to exclude malignancy will be considered.

Patients with locally advanced stage III or stage IV epithelial cancers of the breast will be considered for combined modality trials.

Cancer of the Stomach—Patients with suspected, documented, or locally recurrent **carcinoma of the stomach** may be considered for treatment under combined modality surgery-radiation therapy protocols.

Esophageal Cancer—Patients with untreated potentially resectable **epidermoid cancers or adenocarcinoma** of the middle and lower third of the esophagus will be considered for combined surgery-chemotherapy trials.

Melanoma—Patients with **malignant melanoma** suspected of having regional lymph node metastases but who have not had a regional lymph node dissection will be considered for trials evaluating the effectiveness of monoclonal antibodies in the detection of lymph node metastases.

Bladder Tumors—Patients with suspected or documented invasive **bladder carcinoma.** These patients may be considered for treatment on combined modality surgery-radiation therapy protocols.

Lung Cancer—Patients with **squamous cell carcinoma of the lung** confined to one hemithorax, and who have had no prior treatment or previous thoracotomy will be considered for combined modality surgery-radiation therapy protocols.

Hepatocellular Tumors—Patients with potentially resectable **hepatocellular carcinoma** who have had no prior therapy will be considered for combined modality surgery-adjuvant chemotherapy protocols.

Bladder Cancer—Patients with suspected or documented **invasive bladder carcinoma** may be considered for treatment or combined modality surgery-radiation therapy protocols. Patients with superficial carcinoma of the bladder will be considered for treatment under combined intravesical Mitomycin C-radiation therapy protocols.

National Institute of Child Health and Human Development

D. Lynn Loriaux, M.D., Ph.D.
Clinical Director

The NICHD is broadly concerned with the biological and neurobiological, medical and behavioral aspects of normal and abnormal human development. Patients with genetic, endocrine, or developmental disorders are admitted to the Institute's inpatient and outpatient services.

Telephone referrals of patients to NICHD studies may be directed to the Office of the Chief of the appropriate Branch. General inquiries may be directed to Dr. Loriaux at (301) 496-4686.

HUMAN GENETICS BRANCH

Chief: Michael A. Zasloff, M.D., Ph.D.
(301) 496-6683

The Human Genetics Branch pursues the diagnosis and treatment of a broad range of inborn errors of metabolism, including **amino acidurias, organic acidurias, lysosomal storage diseases, disorders of carbohydrate metabolism, mucopolysaccharidoses, bone and connective tissue disorders,** and **transport defects.**

Selected patients will be accepted into protocols designed to investigate the following specific disorders:

Cystinosis—Individuals with **nephropathic cystinosis** are treated with cysteamine and other cystine-depleting agents. Growth, kidney function, and effects of cysteamine therapy are monitored. The natural history of cystinosis is being studied in cystinotic patients who have undergone a renal transplant. Individuals with **late-onset** and **benign**

cystinosis, as well as **infants with cystinosis** diagnosed at birth are of special interest. The clinical concomitants of renal **Fanconi syndrome** are being investigated.

Homocystinuria—Patients with **pyridoxine-nonresponsive homocystinuria** are treated with either betaine or placebo in a double-blind crossover study to determine the efficacy of betaine in reducing or preventing **osteoporosis.** (Betaine assists in the metabolic conversion of homocysteine to methionine.)

Lysosomal Storage Disorders—Individuals with suspected but undiagnosed **lysosomal storage disorders** are sought for investigation. Deficiencies of two or more lysosomal enzymes, variant manifestations of a single lysosomal dificiency, and the combination of a **lysosomal enzyme deficiency** with **cystine storage** provide examples of unique metabolic diseases in which diagnosis will be attempted.

Amino Acid Disorders—Selected patients with **aminoacidemias** or **aminoacidurias** of unknown etiology will be investigated in an attempt to provide a diagnosis and possible treatment.

Prader-Willi Syndrome—Patients with **Prader-Willi syndrome** are enrolled in a study comparing them with exogenously obese subjects. Special emphasis is placed on endocrine and CNS control mechanisms, and the effects of dietary maneuvers on weight management.

Glycogen Storage Disease—Individuals with any of the various types of **glycogen storage disease** are managed using cornstarch and other dietary regimens and feeding techniques designed to maximize metabolic homeostasis. Data are accumulated on the clinical manifestations and natural histories of specific types of glycogen disorders.

Abnormal Calcium Metabolism—Patients with known or suspected **abnormalities in calcium and bone metabolism** are investigated using stable isotopes of calcium. The kinetics of calcium disposal *in vivo* are being studied by mass spectrometry.

Mucopolysaccharidoses—Selected individuals with **Hunter, Hurler,** or **Sanfilippo syndromes** may be eligible for transplantation of donor amniotic membrane tissue (which is non-immunogenic). This new technique is being examined to learn if it will provide a mechanism for enzyme replacement.

Osteogenesis Imperfecta—Several types of **osteogenesis imperfecta** are being studied at the level of the gene defect. Collagen-specific nucleotide probes are used to study gene expression in skin and bone. Clinical studies are being conducted on the endocrine basis of **short stature** in osteogenesis imperfecta.

Fibrodysplasia Ossificans Progressiva—Patients with **fibrodysplasia ossificans progressiva** are enrolled in a study testing the efficacy of retinoic acid derivatives in retarding ectopic bone formation. Related bone disorders are examine for comparison and contrast with this disease, as well as for possible therapy.

Fetal Alcohol Syndrome—Patients with **fetal alcohol syndrome** are enrolled in a study of the clinical and biochemical characteristics of this disorder. In particular, the roles of thiamine and thiamine-dependent enzymes in the fetal alcohol syndrome are being investigated.

DEVELOPMENTAL ENDOCRINOLOGY BRANCH

Chief: D. Lynn Loriaux, M.D., Ph.D.
(301) 496-4686

The Developmental Endocrinology Branch directs its efforts toward furthering our understanding of the endocrine concomitants of growth, development and reproduction. Patients of any age are admitted.

Patients with the following disorders are of current interest:

Cushing's Syndrome—Patients with the tentative diagnosis of **Cushing's syndrome** are accepted for

clinical trials designed to assess the diagnostic and therapeutic efficacy of several newly discovered or synthesized hormonal regulators or ACTH secretion.

Precocious Puberty—Patients with **precocious pubertal development** are accepted into protocols studying the pathophysiology of this disorder and evaluating new methods of treatment such as LHRH analogues.

Short Stature—Patients with **short stature** are being treated with newly developed growth factors. The efficacy of these drugs is being compared to standard treatment with growth hormone.

Infertility—Men and women with all types of **infertility** are being studied in protocols evaluating new forms of fertility induction.

Pituitary Tumors—Patients with **pituitary tumors** are being studied to determine the optimum treatment modality for this disease. This study is being carried out in collaboration with the Neurosurgical Branch of the NINCDS.

Ambiguous Genitalia—Children and adults with **ambiguous genitalia** are being evaluated in protocols designed to identify the causes of this disorder. Treatment will be offered where appropriate.

CELL BIOLOGY AND METABOLISM BRANCH

Chief: Richard D. Klausner, M.D.
(301) 496-4953

The Cell Biology and Metabolism Branch is concern with **abnormalities of metal metabolism.** Of particular interest are patients with **hereditary hemochromatosis.** Patients can be referred for diagnosis and clinical evaluation, for recommendations concerning therapy, and for the management of multisystem involvement. Patients and family members are enrolled in studies aimed at understanding the molecular basis of the disease as well as establishing tools for early diagnosis.

LABORATORY OF COMPARATIVE ETHOLOGY

Chief: Stephen J. Suomi, Ph.D.
(301) 496-6833

Developmental Psychology—The Child and Family Research Section of the Laboratory of Comparative Ethology is conducting a series of normative and descriptive studies on children's **behavioral development** and their experiences in the natural home environment. Research participants are from the Washington area. Mother-infant and father-infant interactions are studied through the first year of life. Background events, such as whether the mother is employed outside of the home, are evaluated for their influence on the child's psychological development. Longitudinal studies focus on the events which motivate the child to develop competence, with the period of observation through the first six years of life.

National Institute of Dental Research

BRUCE J. BAUM, D.M.D., Ph.D.
Clinical Director

Telephone referrals of patients to NIDR studies should be directed to the investigators listed after the study description.

Salivary Gland Function and Dysfunction—Patients with suspected or actual **alterations in salivary gland physiology** are needed for participation in projects to evaluate the etiology, sequelae and treatment of such disorders. Particular interest is focused on **idiopathic xerostomia (dry mouth)** such as that thought to be associated with aging or menopause, as well as a dry mouth associated with systemic disease (including Sjogren's or sicca syndrome) or radiation-induced gland damage. Individuals with head and neck neoplasms whose regimen of therapy would consist of radiation of the oro-facial area (independent of chemotherapy) are needed to be seen *before, during* and *after* the course of radiotherapy. Comprehensive oral evaluation and therapy, when appropriate and available, will be provided. Patients with **hypofunctional salivary glands** are sought for clinical trials of agents to increase salivary output.—Philip C. Fox, D.D.S., (301) 496-4278.

Taste and Related Oral Sensory Disorders—Patients who are experiencing **distortions (loss, modifications, etc.) of taste**, independent of suspected etiology, and patients with **olfactory disorders**, or both, are needed for clinical studies. Conditions of interest include those related to salivary gland dysfunction and therapeutic drug regimens, as well as idiopathic disorders. Any patients with a strong family history of taste and/or olfactory disorders would be of special interest. Thorough oral and dental evaluations are made of each patient, and gustatory and olfactory functions are clinically evaluated. Where appropriate, con-

sultation and evaluation by indicated medical specialists will be offered.—James Weiffenbach, Ph.D., (301) 496-4278.

Oral Motor Dysfunction—Individuals with altered performance in orofacial muscular functions (for example, swallowing, mastication, speech, irregular tongue movements), independent of generalized neurologic dysfunction, are needed for studies of the etiology, assessment and treatment of such disorders. **Oral motor dysfunctions** which are drug induced and idiopathic are of most interest. Also, patients with general neuropathies but who exhibit particularly disabling oral motor disorders, will be considered for study. Patients will receive a thorough oral evaluation as well as clinical dental examination. A physical oral motor evaluation will be made and, where applicable, noninvasive, quantitative assessments of tongue functions will be made by ultrasound methodology. Consultation with indicated medical specialists and speech pathologists will be made as appropriate.—Bruce J. Baum, D.M.D., Ph.D., (301) 496-1363.

Recurrent Herpes—Individuals with **recurrent herpes simplex** involving the face or other non-genital areas (e.g. buttocks & thighs) are needed for studies examining the pathogenesis and therapy of these lesions.—Abner L. Notkins, M.D., (301) 496-0309.

Oral Surgery—Patients in need of removal of **impacted third molars** serve as subjects for a series of investigations to evaluate pharmacological methods of pain control. Novel analgesics, local anesthetics and sedative drugs are compared to standard drugs used for these purposes. Patients usually have their third molars on one side removed at one appointment and the remaining two removed at a second appointment approximately two weeks later.—Raymond Dionne, D.D.S., Ph.D., (301) 496-5483 and Ronald Dubner, D.D.S., Ph.D., (301) 496-6804.

Post-herpetic Neuralgia—Patients who have persistent pain at least 3 months after the outbreak of

shingles, or herpes zoster, may take part in controlled trials of a number of classes of drugs. —Mitchell Max, M.D., (301) 496-5483.

Painful Diabetic Neuropathy—Patients with chronic pain from diabetic polyneuropathy or mononeuropathy may take part in controlled trials of conventional and experimental drugs that may relieve pain in this condition.—Mitchell Max, M.D., (301) 496-5483.

Chronic Orofacial and TMJ Pain— Selected patients with chronic orofacial pain and headache, particularly those with myofascial pain, are eligible for several outpatient studies on this class of disorders. All patients will continue their care with the referring physician or dentist. —Elyse Singer, M.D. and Raymond Dionne, D.D.S., Ph.D., (301) 496-5483.

National Eye Institute

CARL KUPFER, M.D.
Acting Director

ROBERT B. NUSSENBLATT, M.D.
Deputy Clinical Director

Telephone referral of patients to NEI studies may be directed to Dr. Nussenblatt at (301) 496-3123.

CLINICAL BRANCH

Cataracts—Patients with **cataracts**, are sought for clinical, biochemical, histochemical and histopathologic correlative studies. Discussion of pupillary membranes with laser pulses is being assessed in selected children and adults.

Glaucoma: Studies of the Factors Controlling Intraocular Pressure—Patients with **glaucoma, pigment dispersion syndrome, essential iris atrophy** and **ocular hypertension** are being studied.

Neuro-Ophthalmology—Patients with various **ocular motor, visual or visuo-congenital disturbances** of intracranial origin are being studied by electro-oculography, pupillography, color testing and campimetric methods to test neurophysiologic principles and diagnostic criteria. Selection of cases is based on individual discussion with the referring physician.

Ophthalmic Congenital and Genetic Disease—Clinical, biochemical, psychophysical and electrodiagnostic studies of patients with retinal diagnostic problems, retinal diagnostic problems, retinal degeneration such as **retinitis pigmentosa, juvenile macular degeneration, fundus flavimaculatus, gyrate atrophy of the choroid** and **retina**, etc., are being conducted. Patients with **inherited ocular disease** or developmental abnormalities of the eye are also sought. Of special interest are patients and families with anterior chamber abnor-

malities such as **Reiger's, Peter's** and **Axenfeld's Syndromes, anridia, oculocutaneous albinism** and **ocular albinism.**

Congenital and Acquired Color Vision Deficiencies—Patients with verified or suspected **alterations of color vision,** either congenital or secondary to retinal or intracranial disorder, are being sought for study of the physiological concomitants of the alterations and to test neurophysiological principles and diagnostic criteria. Selection of cases is based on individual discussion with the referring patient and on preliminary testing.

Vitreo-Retinal Disease—Patients with adult onset diabetes and minimal or no ocular changes are being recruited. This is to test the efficacy of drugs to prevent the ocular manifestations of this disease. Additionally, diabetic patients with ocular changes such as macular edema are being sought to participate in randomized laser studies.

Retinal Degeneration—Patients with **senile macular and other acquired disorders of the macula,** especially **idiopathic central serous choroidopathy,** are being sought for studies of the pathogenesis of these conditions. Patients with **retinitis pigmentosa,** especially members of larger pedigrees, are also being sought for clinical studies. **Macular edema** cases are also of special interest.

Uveitis—Patients having **ocular sarcoidosis, toxoplasmic chorioretinitis, pars planitis, ocular complications of Behcet's disease, Harada's disease, intractable uveitis of unknown cause, severe recurrent anterior uveitis** are being sought for the study of the immunologic concomitants of their disease and for therapeutic clinical trials. Patients with intermediate and posterior **uveitis** are being sought for a double masked randomized study evaluating the efficacy of Cyclosporine to accepted medical therapy.

Corneal Disease—Patients who have had **corneal transplant failures** are also being sought. The efficacy of new drugs to prevent corneal transplant rejection are being studied on these patients.

National Heart, Lung, and Blood Institute

HARRY R. KEISER, M.D.
Clinical Director

Telephone referrals may be directed to the individuals listed under each branch.

CARDIOLOGY BRANCH

Chief: Stephen E. Epstein, M.D.
(301) 496-5817

Hypertrophic Cardiomyopathy (HCM, ASH, IHSS)—Selected patients having or suspected of having HCM are being evaluated and followed medically. Operations will be performed on those patients requiring surgical intervention.

Dilated Cardiomyopathy—Patients under 65 years of age with suspected dilated cardiomyopathy are being admitted for diagnostic and therapeutic evaluation. Patients will be catheterized and undergo myocardial biopsy. If the diagnosis of **dilated cardiomyopathy** is established, the patient will enter a randomized trial to determine the relative efficacy of standard intensive medical therapy versus such therapy accompanied by anti-inflammatory drugs.

Congenital Heart Disease—A broad program in the diagnosis of congenital heart disease is in progress. Selected patients with most forms of congenital heart disease amenable or potentially amenable to correction are accepted for diagnostic study. Of particular interest are children and adults suspected of having **atrial** or **ventricular septal defects, congenital aortic stenosis** or **tetralogy of Fallot.**

Coronary Artery Disease—Patients under 65 years of age with **angina pectoris** are being studied by clinical techniques, exercise testing, radionuclide cineangiography and coronary arteriography in

order to select appropriate candidates for surgical correction or balloon dilation. In addition, a prospective natural history study of patients with CAD and mild or moderate symptoms is in progress to determine whether high-risk and low-risk subgroups can be identified (by coronary angiography, radionuclide cineangiography, exercise testing, 24-hour ECG tapes, etc.). Such information could then be applied to considerations relating to prophylactic coronary bypass operation. Patients with unstable angina are also being studied to determine whether they are candidates for fibrinolytic therapy of PTCA.

Dynamic Coronary Obstruction—Patients with anginal-like chest pain and normal coronary arteries are being evaluated by noninvasive and invasive techniques to determine whether the pain is due to myocardial ischemia and, if so, to ascertain the precipitating mechanisms and optimal therapeutic approaches.

Valvular Heart Disease—An investigation designed to determine the optimal time for operative intervention is being conducted in patients with **aortic or mitral valvular disease** of rheumatic or congenital origin. Surgery will be performed in those patients requiring surgical correction, and studies will be conducted to determine those (echocardiographic, radionuclide, hemodynamic) measurements that most reliably reflect reversible or irreversible myocardial dysfunction.

HYPERTENSION-ENDOCRINE BRANCH

Chief: Harry R. Keiser, M.D.

Hypertension and Hypotension
(301) 496-1518

As part of a broad program for the study of blood pressure control, this branch will admit for diagnosis, study and treatment, patients with **hypertension** and **hypotension** of whatever cause. Under special study are:

Essential Hypertension—The pathologic physiology of **idiopathic hypertension** is under intensive

study in a number of laboratories of the branch, and a program is in progress to explore new pharmacological agents and regimens. Patients under 55 years of age without advanced degenerative changes are preferred. This branch is currently seeking patients under the age of 40 who have hypertension and require dental work such as third molar or other extractions.

Familial Hypertension—Patients with ACTH-dependent (Laidlaw) **hypertension** or the low-renin, low-aldosterone variety (Liddle) or with the DOCA-dependent either without (Biglieri) or with 11-hydroxylase deficiency (adrenogenital) are being accepted.

Pheochromocytoma—A broad study of the biogenesis and pharmacology of epinephrine and norepinephrine which will contribute directly and indirectly to diagnosis and treatment is under way. In established cases, definitive therapy for either benign or malignant disease is available at the request of the referring physician.

Postural Hypotension—A study of the altered sympathetic nervous system and the function of the adrenal cortex and of the role of vasodepressor agents in this disorder is in progress in an effort to clarify the mechanisms and improve therapeutic measures.

Renovascular Hypertension—**Disorders of renin production and release** are under investigation. In established cases of renovascular hypertension, definitive therapy is available at the request of the referring physician.

Steroid Hypertension—All forms of **steroid hypertension** are studied, including **aldosteronism, Cushing's syndrome, DOCA hypertension and the hypertension resulting from enzymatic deficiency or block (17-hydroxylase, 11-hydroxylase) in adrenal steroidogenesis.** The control of adrenal steroid biogenesis and the mechanism of steroid hypertension are subjects of several current investigations.

Sympathetic Nervous System Hyperactivity—Detailed studies of amine metabolism and drug effects are in progress in patients with clinical signs of **hyperactivity of the sympathetic nervous system.** Other manifestations under study include **labile hypertension, cutaneous flushing, tachycardia, and diaphoresis,** particularly in young individuals without demonstrable disease.

Other Areas of Interest

Diabetes Insipidus and the Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH)—An examination is being made of the mechanisms of urine dilution and concentration in patients with true **diabetes insipidus.** Selected patients with SIADH are being evaluated for the factors underlying the development of the disorder, especially in relation to renal handling of salt and water and the action of pharmacologic agents.

Hypokalemia—Patients with **hypokalemia,** whether or not associated with hypertension, are admitted for diagnosis and treatment. Patients with **hypokalemia,** normal blood pressure hyperreninemia and **aldosteronism** are being extensively studied to determine if they have a tubulopathy such as Bartter's syndrome, magnesium-losing tubulopathy or calcium-losing tubulopathy or other cause of their abnormal renal function. Full diagnostic facilities are offered and assistance with management is available as desired.

MOLECULAR DISEASE BRANCH

Chief: H. Bryan Brewer, Jr., M.D.
(301) 496-5095

Hyperlipidemia (Hyperlipoproteinemia)—A long-range clinical study is being conducted, on an inpatient and outpatient basis, of patients with **hypercholesterolemia, hypertriglyceridemia** or both. Familial cases and acquired **hyperlipidemia (secondary to diet, dysglobulinemia, obstructive liver disease and certain other causes)** may be accepted. Both etiology and therapy are under investigation. Criteria: abnormally high cholesterol

or triglycerides concentrations or xanthomatosis, especially when familial. Patients with early vascular disease are of special interest.

Hypolipidemia (Hypolipoproteinemia)—Familial disorders associated with **deficiency of one or more lipids** are being intensively studied. These include **abetalipoproteinemia, hypobetalipoproteinemia, alpha lipoprotein deficiency (Tangier disease), lecithin:cholesterol acyltransferase deficiency (plasma cholesterol ester deficiency).** Criteria: acanthocytes, very low concentrations of plasma cholesterol, cholesterol esters, triglycerides or foam cells in tonsils or other tissues.

CLINICAL HEMATOLOGY BRANCH

Chief: Arthur W. Nienhuis, M.D.
(301) 496-5093

Sickle Cell Anemia and Thalassemia—This program of investigation is focused on pharmacological manipulation of fetal hemoglobin synthesis. Clinical trials are designed to determine the ability of various drugs to increase HbF production and to evaluate the hematological and clinical effects of increased HbF. Molecular and cellular mechanisms of induced HbF synthesis are investigated in the laboratory using bone marrow cells obtained from patients under drug treatment. Several noninvasive methods for defining the pathophysiological mechanism of **sickle cell anemia** and evaluating clinical severity and therapeutic intervention are under active investigation. Patients with secondary hemochromatosis due to prolonged transfusion are candidates for chronic chelation therapy. The value of such therapy is investigated using noninvasive measures of tissue iron deposition and toxicity.

Aplastic Anemia and Other Syndromes of Bone Marrow Failure—Patient with **aplastic anemia** are accepted for various therapeutic studies including administration of antithymocyte globulin and the antiviral agent, acyclovir. The pathogenesis of aplastic anemia is being investigated. Patients with **pure red cell aplasis, sideroblastic anemia, parox-**

ysmal noctural hemoglobinuria, and other **myelodysplastic syndromes** are accepted for study and possible treatment.

Chronic Myelogenous Leukemia—Patients in chronic phase of their disease are accepted for study. The use of interferon for treatment is being investigated. *In vitro* laboratory studies are designed to find the genetic basis for this syndrome and for its evolution to acute leukemia.

PULMONARY BRANCH

Chief: Ronald Crystal, M.D.
(301) 496-1597

Interstitial Lung Disease—Clinical studies in the pathophysiology and biochemistry of **pulmonary interstitial disease** are underway. Patients with roentgenographic evidence of interstitial disease and/or evidence of restrictive disease by pulmonary function testing are being accepted for diagnostic studies. Patients with known diagnoses are accepted on an inpatient and outpatient basis as part of a long-range study in the natural history and therapy of these disorders. Particular emphasis is placed on **idiopathic pulmonary fibrosis, sarcoidosis, hypersensitivity, pneumonitis, inorganic dust diseases (pneumoconioses), drug-induced disease and chronic eosinophilic pneumonias.**

Hereditary Emphysema (α-1 Antitrypsin Deficiency)—Patients homozygous and heterozygous *for the* **Z-type α-1 antitrypsin deficiency associated emphysema** are being accepted for diagnostic and therapeutic studies.

Alveolar Proteinosis—Studies on these patients are being conducted with emphasis on physical and chemical characteristics of lavage fluid.

Pulmonary Emphysema—Patients with mild to moderate **emphysema** without a history of chronic bronchitis are being accepted as a part of the ongoing study of the role of inflammation in destructive lung disease.

Pulmonary Lymphangioleiomyomatosis—Clinical studies in the pathophysiology and lymph dynamics are under way as part of a large-scale study of the interstitial lung diseases.

Eosinophilic Granuloma of the Lung Histiocytosis-X—Patients with clinically suspect or biopsy proven eosinophilic granuloma are being accepted as part of a physiologic and therapeutic study.

SURGERY BRANCH

Chief: Richard E. Clark, M.D.
(301) 496-4285

Surgical Treatment of Complex Congenital Heart Disease—Patients with severe forms of **tetralogy of Fallot**, transposition complexes, and other complex malformations amenable to extensive reconstructive procedures are under investigation in an effort to develop more durable operations. Advanced noninvasive studies of RV-PA conduits and new pharmacologic interventions for pulmonary hypertension are in trial as part of long-term studies of right ventricular dysfunction.

Idiopathic Hypertrophic Subaortic Stenosis—Intraoperative ultrasonic studies are in use for immediate definition of applicability and result of septal myectomy. An alternative treatment program of mitral valve replacement is in progress.

Coronary Artery Disease—Patients with moderate disease are accepted for studies of coronary vascular resistance before and after coronary artery procedures. Physiologic definition of the role of endarterectomy is under investigation. New operations for augmentation of cardiac blood flow will be initiated for patients with poor coronary artery anatomy without extensive myocardial destruction.

Acquired and Congenital Valvular Disease—Patients are accepted for a variety of programs for special study. These include investigation of membranous subaortic stenosis, new approaches to valvular regurgitation including use of reconstructive techniques and trials of new valvular prostheses.

National Institute of Mental Health

REX W. COWDRY, M.D.
Clinical Director

Telephone referrals of patients to NIMH studies may be directed to the individuals listed under each subject area.

Depression and Mania—A wide range of studies in the psychobiology of **affective disturbance** is under way, including studies on alterations in biogenic amine metabolism, electrolytes, neuroendocrine function and disturbances in biological rhythms. In addition, a number of psychosocial and psychodynamic factors in depression and suicide are under investigation.

Programs are available for both inpatients and outpatients, and may involve an evaluation with biological studies and recommendations, an evaluation with treatment in collaboration with the referring therapist, or a full evaluation and treatment program. Patients with **endogenous depressions** and/or **bipolar affective disorder** are usually eligible for participation. Specific studies address rapid-cycling, seasonal, or menstrually related mood disorders. The eligibility of individuals with more atypical presentations depends on the specific history and symptoms and on the status of specific research studies. Because of the wide variety of evaluation and treatment programs, referring physicians may call (301) 496-1337 or write the Office of the Clinical Director (Attn: Kathy O'Leary, MSW) to determine the most suitable program.

There are a wide range of treatments under investigation in both inpatient and outpatient studies. Pharmacologic studies of standard and investigational antidepressants, lithium, and carbamazepine are on-going. Non-pharmacologic interventions such as sleep-derivation and circadian shifts are used in other studies. Individual, family, group and milieu therapies may be employed in the treatment program.

Genetic studies are being conducted in selected families with a history of affective illness. Family members are evaluated using a number of clinical and biochemical parameters to try to determine heritable as well as social factors that contribute to the development of affective illness. In addition, participating families are examined for possible "linkage" between known chromosomal markers and affective illness in the hope of further clarifying the mode(s) of transmission within families. —Kathy O'Leary, M.S.W., Office of the Clinical Director, (301) 496-1337.

Obsessive-Compulsive Disorder—This institute is conducting a comprehensive investigation into the psychobiology of adults with **obsessive-compulsive disorder.** Major areas of research interest include (1) developing clinical assessment measures for the phenomenology of the disorder (2) identifying neurological correlates of obsessions and rituals and (3) comparing the therapeutic efficacy of a monoamine oxidase inhibitor and a tricyclic compound.

This investigation will involve both inpatients and outpatients, with inpatients receiving individual, group and family therapies in the setting of a therapeutic milieu. In particular cases, arrangements can be made for brief hospitalizations to permit completion of neurological, psychophysiological and biochemical tests prior to an extended outpatient drug trial. For both inpatients and outpatients, the institute is interested in studying the families of people with this disorder.—Thomas R. Insel or Joseph Zohar, M.D., Laboratory of Clinical Science, (301) 496-2757.

Borderline Personality Disorder—A pilot study is under way to examine a select group of women, ages 18-35, who have been diagnosed as borderline and who show marked **dysphoria** following real or perceived rejection. The evaluation includes electroencephalographic studies during a clinical interview. All patients must be in ongoing psychotherapy with the referring therapist. Treatment recommendations will be made to the referring psychiatrist after the evaluation.—Kathy O'Leary, M.S.W., Office of the Clinical Director, (301) 496-1337.

Schizophrenia—The psychobiology of both acute and chronic **schizophrenia,** is being explored using clinical, pharmacological, biochemical, neurophysiological and genetic methods. Areas of study include: (1) the dopamine hypothesis of schizophrenia; (2) the biological predictors of response to antipsychotic drugs and the effects of these drugs on brain amine metabolism and neuroendocrine function; (3) the role of peptides in schizophrenia; (4) changes in brain structure and function, using PET, NMR, and cerebral blood flow; and (5) innovative therapeutic modalities.

Of further interest are: (1) the study of persons adopted at an early age who have a biological or adoptive parent who is schizophrenic; and (2) studies to identify possible genetic markers in schizophrenia that may help to predict which offspring are vulnerable to the illness and thus provide a basis for early intervention.

One clinical research unit at the Clinical Center in Bethesda and three clinical research units at the William S. White Building at St. Elizabeths Hospital have been established to provide hospital treatment including individual, family, milieu, group and drug therapy for patients with schizophrenia. Admission of patients early in their psychotic episodes is desirable and can be arranged rapidly.—Judith Schreiber, M.S.W., Clinical Neuroscience Branch at the Clinical Center, (301) 496-6295 or, at the William A. White Building, Carol Rodeffer, M.S.W. (202) 373-7649.

Disorders of Attention and Cognition—Studies of disorders of attention, learning and memory in a variety of populations of patients with **mood disorders, schizophrenias, learning-disabled children, epilepsy and various forms of dementia** are ongoing. The psychobiology of attention and other cognitive processes are examined using a variety of neuropsychological methods, including evoked response, psychophysiological techniques and learning-memory procedures.—Laboratory of Psychology and Psychopathology, (301) 496-2551.

Sleep Disturbances—Relations between psychiatric problems and electroencephalographic patterns of sleep are being intensively studied in several diagnostic groups with special emphasis on pri-

mary **insomnia.** Selected inpatients and outpatients are serially studied while receiving treatment. The role of disturbed 24-hour biological rhythms in **sleep disturbances** is being investigated, and non-pharmacologic manipulations of 24-hour rhythms are being assessed as a treatment strategy for insomnia.—Clinical Psychobiology Branch, (301) 496-1056.

Childhood Mental Illness—Several studies have been initiated related to the psychobiology of **hyperactive children.** Children who are admitted, partially on a day basis, participate in a highly structured, comprehensive diagnostic program that includes medical, neurological and psychiatric evaluations, psychological testing and evaluation of psychomotor and psycholinguistic development. Pharmacokinetic and metabolic studies of psychoactive drugs, psychobiological studies involving sleep and neuroendocrine parameters and clinical studies involving FDA-approved experimental drugs are ongoing.

Other studies involve consultative followup of children in the inpatient program as well as children with **obsessive-compulsive disorder.** Children of adults who have previously been admitted for affective illness will be evaluated for **depression.** Both psychological parameters and the search for biological factors that may serve as "genetic markers" are being investigated. Clinical pharmacological studies of these groups are also ongoing.

Patients with certain forms of genetically determined metabolic alterations are occasionally admitted for biochemical study.—Walter Sceery, M.S.W., or Marge Coffey, M.S.W., Child Psychiatry Branch, (301) 496-6081.

Developmental Psychology—Behavioral studies of children are in progress relating to the effects of stressful biomedical or psychosocial conditions on the functioning of children. Social, emotional and intellectual competencies and disturbances are investigated. The biomedical conditions studied include **juvenile diabetes, cancer** and **malnutrition.** Studies are also being conducted on the effects of parental and family pathology on child behavior. The rearing environments of these children and

also the children's disabilities and coping skills are being investigated intensively. The risk groups are children with a mentally ill parent and children whose mothers are incarcerated. In all of this research, studies of normal child development and rearing are included.

Studies of the development of altruistic and aggressive behavior in children are also underway.

A standardized system is being developed to assess patterns of problem behavior in children from 4 to 16 years of age for both sexes. Studies using this standardized system will be used to evaluate the effectiveness of different kinds of therapies for various behavior disturbances among children.—Laboratory of Developmental Psychology, (301) 496-1091.

Anxiety Disorders—Patients with **panic disorder, agoraphobia,** and generalized **anxiety disorder** are accepted for intensive medical and neuropsychiatric evaluation and assessment of the phenomenology and longitudinal course of their illness. Selected patients with concurrent medical problems such as complex partial seizures, mitral valve prolapse, hypertension and thyroid dysfunction are accepted if anxiety represents a prominent component of the clinical syndrome. Selected patients with a history of cocaine or caffeine-related panic attacks are accepted. Depressed patients with panic attacks and/or agoraphobia will be studied. The institute is interested in studying the children of patients with panic disorder. In addition, a limited number of children with primary anxiety disorders will also be studied. Facilities are available for both inpatients and outpatients. The inpatient unit is reserved for patients with either incapacitating agoraphobia or daily panic attacks; patients requiring rapid evaluation or detoxification from benzodiazepines also may be studied on the inpatient unit. Most patients, however, are treated on an outpatient basis in the Ambulatory Care Research Facility (ACRF). Clinics are presently available on Tuesdays (6pm-9pm) and from 9am-4pm on Wednesdays and Fridays. Treatment modalities may include drugs or individual, family or group psychotherapy. Pharmacotherapy may include conventional and/or research drugs. Extensive

behavioral modification techniques are not employed presently by the institutes' staff.—Barbara Scupi, Biological Psychiatry Branch, (301) 496-6826.

Menstrually-Related Mood and Behavioral Disorders—The Consultation-Liaison Service and Biological Psychiatry Branch are evaluating women who experience **menstrually-related mood or behavioral disorders.** This is accomplished by means of clinical interviews, self-rating scales, and periodic evaluation of mood and endocrine function. Patients who experience well defined menstrually-related mood syndromes may participate in a study designed to evaluate the efficacy of several therapeutic agents—progesterone suppositories, synthetic progestins, Vitamin B6, and carbamazephine—in the treatment of menstrually-related mood disorders. Evaluation of these agents will include periodic interviews, blood studies, and daily symptom self-rating scales. All patients will have completed a baseline evaluation period prior to participating in the treatment study. The duration of the entire evaluation and treatment series may last between six and twelve months. Women must meet the following criteria for acceptance into these studies: (1) history within the last two years of at least six months of menstrually-related mood or behavioral disturbances of at least moderate severity, i.e., disturbances distinct in appearance and associated with a notable degree of subjective distress; (2) symptoms have a sudden onset and offset; (3) age 18 to 65; (4) not pregnant and in good health; (5) not on medication; (6) regular menses.—Anne Bowles or Chris Hoban, Consultation-Liaison Service, (301) 496-9675.

Premenstrual Syndrome (PMS)—The Clinical Psychobiology Branch is studying individuals with **premenstrual syndrome (PMS),** in which changes in mood, behavior, cognition, and physical well-being occur during the premenstrual phase of a woman's menstrual cycle and are severe enough to disrupt normal functioning in work and social spheres. The branch conducts studies which examine sleep, temperature, activity patterns across the menstrual cycle in women with PMS and in

normal controls. Treatment strategies involve alteration of sleep schedules and exposure to high intensity light in order to try to correct disturbances in sleep and hormonal rhythms and to effect clinical remission. To be eligible for these studies an individual must be between the ages of 20 and 45, have regular menstrual cycles, and be on no psychoactive medication.—Robert Skwerer, M.D. Clinical Psychobiology Branch, (301) 496-2141.

Eating Disorders—Patients with **anorexia nervosa** and **bulimia** are being studied from the standpoint of neuroendocrine and neurotransmitter function and treatment response. Treatment approaches include behavioral and drug therapy. Present protocols involve primarily inpatients, although studies of bulimia will include outpatients.—Section on Experimental Therapeutics, (301) 496-1891.

Alzheimer's Disease—Individual patients with twins with early or moderate **dementia** of the **Alzheimer's** type are being evaluated in a wide variety of studies within the Institute. The Alzheimer program consists of both inpatient and outpatient evaluations, but the centerpiece of the dementia program is the inpatient unit where patients are assessed in a comprehensive manner from both a phenomenologic and biologic perspective. In addition to routine diagnostic and neuropsychologic assessment, testing using drugs as well as therapeutic agents affecting the cholinergic and other brain neurotransmitter systems are currently in use. Attempts are also being made to better understand the depressive features of dementia by the introduction of new assessment tools specifically designed to this population. For relatives, much emphasis is placed on the stresses that Alzheimer's disease places on the family as a whole and the new coping mechanisms required. All participants and their families are encouraged to remain involved in the longitudinal follow-up studies once they have completed the initial inpatient evaluation.—Trey Sunderland, M.D., Clinical Neuropharmacology, (301) 496-2757.

National Institute of Neurological and Communicative Disorders and Stroke

MARK HALLETT, M.D.
Clinical Director

Telephone referrals may be directed to the individuals listed under each branch.

DEVELOPMENTAL AND METABOLIC NEUROLOGY BRANCH

Chief: Roscoe O. Brady, M.D.
(301) 496-3285

Associate Chief
John A. Barranger, M.D., Ph.D.
(301) 496-1465

Sphingolipidoses, Mucopolysaccharidoses and Storage Disorders—Patients with **Gaucher's disease, Tay-Sachs disease, Niemann-Pick disease, metachromatic leukodystrophy, Krabbe's disease, Fabry's disease,** as well as those with the various types of **mucopolysaccharidoses,** are currently being studied. Diagnosis of the disease and carrier state is available. Genetic counseling and antenatal diagnosis is offered. Basic biochemical and molecular genetic studies are carried out on selected patients. Clinical studies of enzyme replacement and bone marrow transplantation are being conducted.

Neurologic Disease with Metabolic Abnormalities—A few patients are selected for diagnosis, study and therapy. Of particular interest are patients with known or suspected **Refsum's disease Menke's disease, Wilson's disease, adrenoleukodystrophy (Schilder's disease), ceroid lipofuchsino**

sis and the **heredofamilial acute or progressive ataxias.**

Progressive Dementia in Children—Infants and children suffering from **delayed development spasticity** and signs of progressive **dementia** with or without seizure disorders will be considered for admission for diagnosis, investigation and therapy if possible. Genetic counseling and detection of carrier states is offered where a metabolic defect is identified. A few patients will be accepted for basic and clinical research studies.

NEUROIMMUNOLOGY BRANCH

Chief: Dale E. McFarlin, M.D.
(301) 496-1801

Assistant Chief: Henry F. McFarland, M.D.
(301) 496-1801

Multiple Sclerosis—A few patients with early disease are selected for highly specific immunologic and virologic studies.

Familial Multiple Sclerosis—Genetic, immunologic and virologic studies are being conducted in families with unequivocal occurrence of **multiple sclerosis** in more than one individual. Monozygotic and dizygotic twins who are discordant or concordant for MS are being admitted.

Myasthenia Gravis— This and other neuromuscular disease patients with **myasthenia gravis** are being admitted for evaluation of immune function. A few patients with neuromuscular diseases such as **dysimmune neuropathies** and **inflammatory myopathies** are being studied.

Subacute Sclerosing Panencephalitis—A few patients are being accepted for basic immunologic investigation.

EXPERIMENTAL THERAPEUTICS BRANCH

Chief: Thomas N. Chase, M.D.
(301) 496-7993

Extrapyramidal Disorders—Individuals with **Parkinson's disease** and related disorders with parkinsonian symptoms including **progressive supranuclear palsy** and **striatonigral degeneration** as well as those with **Huntington's disease, tardive dyskinesia, Tourette syndrome, torsion dystonia** are admitted for diagnosis, biochemical study, and experimental drug therapy. Investigations are conducted both on an inpatient and outpatient basis.

Dementing Disorders—Patients with **Alzheimer's disease** and related presenile or senile dementias, including **multi-infarct dementia** and **Pick's disease**, are accepted for diagnosis, pathogenetic study including cerebral imaging with positron emission tomography, and experimental therapeutic interventions.

Essential Tremor—Selected individuals with **familial, senile, or idiopathic action tremor** are accepted for study.

Cerebellar Ataxia—Patients with **olivopontocerebellar atrophy** or related **cerebellar ataxias** are admitted for diagnosis, biochemical evaluation, and treatment.

SURGICAL NEUROLOGY BRANCH

Chief: Paul L. Kornblith, M.D.
(301) 496-5728

Brain Tumors—The cellular biology, immunobiology and radiobiology of **glial and other central nervous system tumors** are being studied with respect to the biologic and pathologic characterization as well as the therapy of individual tumors. Basic to these studies is the tissue culture of patient tumors. Patients with malignant gliomas are being sought for operative removal of tumor and subsequent characterization of tumor properties. A comprehensive program of therapy is available for

these glioma patients including innovative radiotherapy (radiosensitizer and interstitial brachy therapy), chemotherapy (intraarterial therapy with protection of the bone marrow by drug removal as well as systemic chemotherapy with standard as well as phase I agents and immunotherapy (intratumoral interleukin 2 stimulated lymphocytes).

Spinal and Intracranial Arteriovenous Malformations—Patients for diagnostic angiography and surgery are appropriate for referral.

Pituitary Tumors—**Pituitary tumors** are being studied. Special emphasis is being placed on pathologic characterization, including malignant potential as well as identification of specific peptide production. Referrals of patients with microadenomas as well as larger pituitary mass lesions (including those with suprasellar extension) are being sought.

INFECTIOUS DISEASES BRANCH

Chief: John L. Sever, M.D., Ph.D.
(301) 496-5881

Congenital Infections—A few pregnant women and newborn children with unusual infections, including **rubella, cytomegalovirus, herpes, toxoplasmosis and varicella** are being accepted for virologic and immunologic studies.

Chronic Infections—A few patients are being accepted for virologic and immunologic studies of **subacute sclerosing panencephalitis, progressive rubella panencephalitis and progressive multifocal leukoencephalopathy** and neurological complication following **Epstein-Barr virus infections** and other **herpes viruses.**

Motor Neuron and Neuromuscular Diseases—Patients with hyperexcitable states of the motor neuron (fasiculations, myokymia, myotonia, cramps and related conditions), Moebius syndrome, atypical motor neuron diseases, and unusual or diagnostically difficult neuromuscular diseases are currently being investigated. Patients receive detailed clinical electrophysiological and, when appropriate, histological evaluations.

Cerebral Evoked Potentials—Patients with various neurological diseases are sought for studies of visual, auditory and somatosensory cerebral evoked responses.

MEDICAL NEUROLOGY BRANCH

Chief: Roger J. Porter, M.D.
(301) 496-9526

Epilepsy—Patients with intractable epilepsy, especially those with partial seizures, may be candidates for drug treatment or surgery. Fundamental studies of the brain which involve a series of projects employing surgical, psychological, neurological, and neurophysiological procedures, are conducted. Patients who are candidates for surgery are studied by an integrated group of neurologists, neurosurgeons, neuropsychologists, and electroencephalographers.

Autonomic Nervous System Disorders—Patients with **neurogenic orthostatic hypotension, autonomic neuropathy,** and neurological diseases attended by **autonomic dysfunction** are accepted for biochemical and pharmacological studies. These studies are designed to investigate the pathophysiology and consequences of chronic autonomic failure. Conventional and experimental treatment of orthostatic hypotension is available.

Involuntary Movement Disorders—Selected patients with **Gilles de la Tourette syndrome** and **dystonia musculorum deformans** are accepted for research protocols involving measurements of neurotransmitter metabolism.

Familial Alzheimer's Disease—Biochemical and genetic studies are conducted on patients with **familial Alzheimer's disease** and their at-risk relatives.

Voluntary movement disorders— Patients with **stroke, parkinsonism and cerebellar ataxia** are accepted for physiological studies with a goal of understanding the mechanisms for the deranged movements. Patients undergo extensive clinical testing and physiological investigations include

electromyographic studies, evoked potential studies, and PET scanning. Patients will be offered therapy as appropriate and some patients with stroke followed serially will get rehabilitative therapy.

Involuntary movement disorders—Patients with **action tremors** which are refractory to conventional therapy are entered into therapeutic drug trials. Patients with **myoclonus** are studied physiologically, classified and offered appropriate therapy. Patients with **hemifacial spasm, blepharospasm,** and **focal dystonia** such as writer's **cramp** are evaluated and given experimental therapy.

Speech Pathology Unit

Speech Pathologist: Christy L. Ludlow, Ph.D.
(301) 496-9365

Speech Disorders—Patients with speech production problems associated with neurological or laryngological disorders or without apparent cause, are being studied for projects investigating movements of the larynx, tongue, lips and jaw during speech and oral movement. Diagnosis and evaluation are available. The effects of timing control and neuropharmacological treatments are being evaluated in selected patients with the following disorders: **dysarthria, verbal apraxia, dystonia, Parkinson's disease, Huntington's chorea, cerebellar disorders, and essential tremor.**

Voice or Laryngeal Disorders—Patients with phonatory disorders associated with neurological or laryngological disorders or without apparent cause, are being studied. Comprehensive diagnostic evaluations are provided. Investigations include vocal fold movements and vibration, respiratory coordination and intrinsic laryngeal muscle function. The effects of intramuscular injections, nerve block and neuropharmacological treatment are being determined for a few patients with the following disorders: **spastic or spasmodic dysphonia, stuttering, vocal fold paralysis, laryngeal nodules or polyps, laryngeal carcinoma and phonatory tremor.**

Clinical Center

JOHN L. DECKER, M.D.
Director

CRITICAL CARE MEDICINE DEPARTMENT

Telephone referrals may be directed to the individuals listed for each protocol.

Idiopathic Dilated Cardiomyopathy and Myocarditis—Patients with moderate or severe heart failure due to a **dilated congestive cardiomyopathy** are eligible if they have no other known heart disease and no systemic disease. Evaluation will include a transvenous myocardial biopsy, and patients will then be randomized with an anti-inflammatory regimen or conventional therapy.—Joseph E. Parrillo, M.D., Critical Care Medicine, (301) 496-9565.

Acquired Immune Deficiency Syndrome—The etiology, pathogenesis and treatment of AIDS is being investigated in a collaborative project with the Medicine Branch, National Cancer Institute, and Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases. Patients with documented HTLV-III infection who are clinically stable can be considered for immunotherapy, treatment of specific tumors, treatment of certain infectious complications, or treatment of the underlying HTLV-III infection.—Henry Masur, M.D., Critical Care Medicine, (301) 496-9565.

INTERINSTITUTE MEDICAL GENETICS PROGRAM

Patient referrals may be directed to Sandra Schlesinger, Clinical Coordinator (301) 496-1380 or Program Directors, John Mulvihill, M.D. or Dilys Parry, Ph.D., (301) 496-4947.

The Interinstitute Medical Genetics Program is a cooperative undertaking involving clinical branches and research laboratories of nine Institutes. Over a dozen senior investigators working on various genetic diseases participate in our clinical on a regular basis, seeing patients of particular research interest to them and serving also as consultants for other patients. In addition to those patients who clearly fall within a research protocol, our Genetics Clinic also accepts referrals of patients requiring diagnostic assessment and genetic counseling for all categories of known or suspected genetic disorders, including chromosomal abnormalities, congenital malformations and biochemical defects. Prenatal diagnosis can be arranged if indicated.

Participating investigators include those with expertise in: inborn errors of metabolism, cytogenetics, congenital anomalies and malformation syndromes, bone and connective tissue disorders, neurological disorders, eye disorders, and cancer.

The index is carried on the AMA/GTE Telenet Medical Information Network. Quarterly index updates are available on the information network to Telenet subscribers.

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